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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/257,650	02/25/1999	MASAHIKO FUJINO	48194	2632

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EXAMINER	
SHAFER, SHULAMITH H	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/257,650	FUJINO, MASAHIKO	
	Examiner	Art Unit	
	Shulamith H. Shafer, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-54 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-54 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11 July 2006 has been entered.

Amendments and remarks filed with RCE request have been entered. Claims 1-44, 55 and 56 have been canceled. Claims 45-52 and 57 have been amended and amendments made of record. Claims 45-54 and 57 are currently under examination. The pertinent remarks/arguments filed 13 June 2006, will be responded to herein.

The text of those sections of Title 35 U.S. Code not included in this action can be found in the prior Office actions.

Withdrawn Rejections

The rejection of claims 45-54 and 57 under 35 U.S.C. 112, second paragraph as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn, in part, in view of applicant's amendments to the claims.

The rejection of Claims 45-54 35 U.S.C. § 102(b) as being anticipated by Birnbaumer et al., and Green et al., is withdrawn in view of applicant's amendments to the claims.

The rejection of Claims 45-51 and 54 under 35 U.S.C. § 102(b) as being anticipated by Kong et al. is withdrawn in view of applicant's amendments to the claims.

The rejection of claims 45-53 under 35 U.S.C. § 103(a) as being unpatentable over Lebrun et al in view of Choong et al., and further in view of Dower et al., are withdrawn in view of applicant's amendments to the claims.

Objections

Claim 51 is objected to because of the following informalities: an article is missing. The claim recites "the β3 adrenergic receptor is β3 adrenergic receptor gene" at line 2. Additionally, there appears to be a typographical error in the claim; the claim has been amended to recite "the a β3 adrenergic receptor gene," at line 4. Appropriate correction is required.

Maintained/New Rejections

35 U.S.C. § 112, Second Paragraph

The rejection of claims 45-54 and 57 under 35 U.S.C. 112, second paragraph as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are maintained for reasons of record and those outlined below.

Claims 45, 46, and 52-54 are indefinite because they recite methods using such terms as "substantially changed affinity" without clearly defining the boundaries of what is meant by the term.

Applicants have traversed (in Response of 13 June 2006, page 6) the rejection of the claims under 35 U.S.C. 112, second paragraph for reciting "substantially changed affinity". The reason for the traversal is that the specification defines substantial change by a functional characteristic, i.e., the ability to cause a disease". Applicant's arguments have been fully considered but are not found to be persuasive for reasons of record as set forth in the previous office action and for the following reasons. The specification

does define "'substantial change' as..... a change to the extent that a disease can be caused and may be any change, whether significant or insignificant, as long as it is capable of causing a disease." However, the specification has not established a nexus between the aberrant receptor (the β3 adrenergic receptor, as now recited in the amended claims) and any disease or pathology. Thus, one would be unable to determine what type of change applicant intends to specify in the claims of the instant invention.

Additionally, the claims recite the terms "operating" (Claim 45), "operational activity" (Claim 52), and "operates" (Claim 53); these terms are not explicitly defined in the specification. It is unclear whether applicant intends the phrases to read as "activating", "stimulating", or something else entirely; therefore the rejection is maintained.

Claim 46 (d) has been amended to recite "selecting a substance that is an agonist or antagonist of the β3 adrenergic receptor". It is not clear at which step in the method of Claim 45 step d is to be performed nor how it relates to steps a-c of claim 45.

Claim 47 is an incomplete sentence; the claim is therefore vague and indefinite and recites insufficient method steps. The claim recites "the method of claim 45 which is suitable for.....". It is unclear how this further limits the method of claim 45. Furthermore, the claim recites "a β3 adrenergic receptor"; it is unclear if applicants intend this receptor to be the wild-type or the mutant form of the receptor. The claim recites "selecting a substance.....". It is unclear how this step relates to the method steps of claim 45. It is unclear if applicant intends to select a substance identified by claim 45, or some other substance and how said substance is to be selected.

Claims 48 and 49, as now amended, do not recite method steps. It is unclear how these claims further limit the method of Claim 45. It is not clear how the recitation of what the method is "suitable for" further limits the method of Claim 45.

Claim 52 has been amended to recite method steps that are similar to those recited in the base claim, claim 45. It is unclear when these method steps are to be performed and how they further limit the method steps of Claim 45.

Claim 57 is rejected as being vague and indefinite in reciting "receptor with a Trp substituted for the Arg at position 64". Any reference to a sequence without a SEQ ID NO: is indefinite because the numbering of residues is not inherent. The sequence disclosed in the specification has a Trp residue at position 64; therefore there is no Arg residue at this position to be substituted for. The specification contemplates a mutation in the β3 adrenergic receptor in which the **Trp residue at position 64 is replaced by an Arg residue** (page 4, lines 30-36, Example 2, 6-8). In the interest of compact prosecution, this claim will be read as "wherein the β3 adrenergic receptor is the human β3 adrenergic receptor with a **Arg** substituted for the **Trp** at position 64 ".

35 U.S.C. § 112, First Paragraph

Claims 45, 57 remain and claims 46-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement as failing to comply with the enablement requirement for reasons of record, as set forth in the previous Office Action, and for reasons set forth below.

Pietri-Rouxel et al., as cited in the previous office action, teach that the affinity of the [Arg64]β3-adenoreceptor for CGP 12177A, a specific β3-adrenoceptor agonist, was indistinguishable from that of the wild-type receptor (page 1176, column 1, 1st paragraph, and page 1175, Table 1). Candelore et al. (1996, Endocrinology. 137:2638-2641) teach that " a careful analysis of the *in vitro* pharmacological properties of the W64R mutant β3 adrenergic receptor has revealed no distinction between the wild type and mutant receptors" (page 2641, 1st column, 1st paragraph). Since the art of record teaches away from the limitations recited in the preamble of Claim 45, the artisan would not be able to make or use this method as recited by the claims of the instant invention.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 45-54 and 57 are rejected under 35 U.S.C. § 102(b) as being anticipated by Candelore et al. (1996, Endocrinology. 137:2638-2641). The claims are drawn to a method comprising: (1) expressing the β3 adrenergic receptor in a cell by gene engineering technology; (2) bringing the receptor into contact with a test substance; and (3) assaying the "operation activity" of the test subject on the β3 adrenergic receptor (Claims 45 and 52). Claim 46 recites the limitation that the substance be an agonist or antagonist to the receptor; Claim 53 is drawn to a substance that normally "operates" the receptor; claim 54 recites the limitation of the "operation activity" being a change in intracellular concentration of cAMP. Claim 57 identifies the β3 adrenergic receptor as the human receptor with a Trp substitituted for Arg at position 64 (interpreted as Arg substituted for Trp, see above).

Candelore et al investigate the effects of the W64R mutation on the pharmacological properties of the cloned human β3 adrenergic receptor expressed in CHO cells. The mutant receptor was expressed in CHO cells (page 2639, 2nd column, 3rd paragraph). Cells were incubated with a number of test substances including ligands for the wild type receptor (page 2639, Table I). The accumulation of cyclic AMP in response to incubation with various test compounds was measured (page 2640, Figure 1). Any study that teaches method steps of expressing a mutant receptor and assaying the functioning of that receptor in response to test compounds would meet the

definitions of a screening assay as recited by the claims of the instant invention. Thus, the teachings of Cardelore et al anticipate all the limitations of claims 45-54 and 57.

Claims 45-54 are rejected under 35 U.S.C. § 102(e) as being anticipated by Emorine al. (2001, U.S. 6,274,706 filed 25 May 1995). The '706 patent teaches various genetically engineered products for testing a variety of chemical agents which may influence the regulation of β3 adrenergic receptors (Column 4, lines 24-28). The reference teaches that the invention encompasses any nucleotide sequence of β3 adrenergic receptors in mammals (column 4, lines 65-67). Variants of the nucleotide sequence include mutations and point substitutions (column 5, lines 2-5). Example 9 teaches the expression of the receptor in eukaryotic cells; example 10 teaches a method of testing chemicals for β3 adrenergic receptor activity, using various concentrations of agonist and measuring the amount of cAMP produced. Thus, the teachings of the '706 patent anticipate all the limitations of claims 45-54.

35 U.S.C. § 103(a)

Claims 45-54 and 57 are rejected under 35 U.S.C. § 103(a) as being unpatentable Emorine et al (the '706 patent) in view of Candelore et al.

The teachings of the '706 patent are discussed in detail above. The '706 reference does not teach a method of testing various chemicals for the ability to activate the β3 adrenergic receptor wherein the β3 adrenergic receptor is the human β3 adrenergic receptor with a Arg substituted for the Trp at position 64. Candelore et al. teach expression of the W64R mutein of the β3 adrenergic receptor in CHO cells and incubating cells with a number of test substances.

Therefore, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of the '706 patent and substitute the mutant β3 adrenergic receptor as taught by Candelore et al. for the β3 adrenergic receptor taught by the '706 patent and use it in a method of testing

various chemicals for ability to activate the receptor. One of ordinary skill in the art would have been motivated to make the modification because the '706 patent teaches that variants of the nucleotide sequence encoding the β3 adrenergic receptor include variants with mutations and point substitutions. One would have expected success because both of the references teach the use of β3 adrenergic receptor variants in the methods of testing various agents.

Conclusion:

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shulamith H. Shafer, Ph.D. whose telephone number is 571-272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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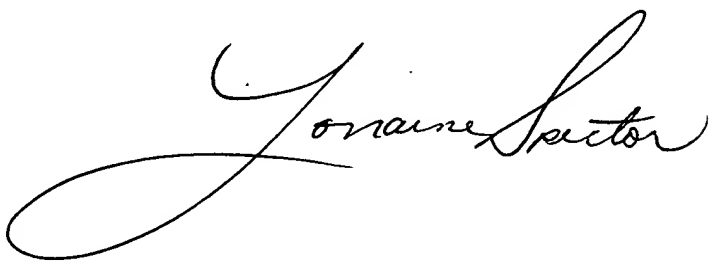

LORRAINE SPECTOR
PRIMARY EXAMINER